REMARKS

Applicants have amended their claims in order to further clarify the definition of various aspects of the present invention. Specifically, claims 1 and 2 have been amended to clarify that the "5' end" included in the primer for introduction is the 5' end "of the primer"; and to recite that the gene to be analyzed is prepared by "introduction of" the first base sequence and the second base sequence comprising a promoter sequence of RNA polymerase, which are nonspecific to the base sequence of the target gene, into the target gene so that the second base sequence is bound to a position closer to a "5' end of the gene to be analyzed" than the first base sequence. Thus, claims 1 and 2 have been amended to provide further clarification of the "5' end" in original claims 1 and 2.

In addition, Applicants are adding new claim 14 to the application. Claim 14, dependent on claim 1, recites that the probe is a DNA/RNA hybrid strand. Note, for example, the paragraph bridging pages 10 and 11 of Applicants' specification.

The restriction requirement set forth on page 1 of the Office Action mailed December 29, 2005, is noted. Applicants affirm their election of the Group I claims, claims 1-9. In addition to claims 1-9, it is respectfully submitted that newly added claim 14 is to be included in the Group 1 claims to be considered on the merits in the above-identified application.

The objection to claim 4 under 37 CFR 1.75(c), set forth in the first paragraph on page 4 of the Office Action mailed December 29, 2005, is respectfully traversed, in view of the following. Thus, claim 3 recites, in step 3), synthesis of the gene to be analyzed from the single-stranded cDNA using the primer for introduction "and DNA polymerase". In contrast, claim 4 recites, in step 3), synthesis of the gene to be analyzed from the single-stranded cDNA using the primer for introduction and "the

reverse transcriptase". Contrary to the conclusion by the Examiner, it is respectfully submitted that claim 4 does not recite "the exact same claim language" as claim 3, differing in the last expression in step 3), and is a proper dependent claim.

Furthermore, note that each of claims 3 and 4 is dependent on claim 1; that is, claim 3 is not dependent on claim 3. Thus, it is not an issue concerning whether claim 4 further limits the subject matter of its parent claim; each of claims 3 and 4 further limit the subject matter of their parent claim 1, and thus each clearly satisfies 37 CFR 1.75(c), as being of proper dependent form.

Applicants respectfully traverse the rejection of their claims under the second paragraph of 35 USC 112, as being indefinite, particularly insofar as this rejection is applicable to the claims as presently amended. Initially, Applicants respectfully traverse the conclusion by the Examiner that the "primer for introduction" is confusing. In this regard, attention is respectfully directed to, for example, pages 3 and 4 of Applicants' specification. As can be appreciated, e.g., in the first full paragraph on page 4, Applicants disclose a primer for introduction, used to introduce the first and second base sequences into the target gene. This primer for introduction is constituted by three sequence portions, also defined in the first full paragraph on page 4 of Applicants' disclosure. Attention is also respectfully directed to Fig. 1 and reference numeral 11, which indicates the primer for introduction (a reverse transcription primer). As described, for example, on page 8, lines 8-15 of Applicants' specification, the primer for introduction 11 is constituted by the sequence portion 12 hybridizing to the target RNA, the sequence portion 13 located closer to the 5' end than the sequence portion 12 and consisting of a sequence identical to the probe for detection, and the sequence portion 14 comprising a T7 promoter sequence located closer to the 5' end than the sequence portion 13.

Continuing in the next paragraph on page 8 of Applicants' specification, it is described that the sequence portions 12, 13 and 14 may be continuous, or there may be a joining portion between two portions. This disclosure on page 8 goes on to describe that the sequence portion 12 varies depending on the target gene sequence, while the sequence portion 13 can be freely designed independent of the target gene sequence and the sequence portion 14 is also independent of the target gene sequence and designed to comprise a promoter sequence or the transcription initiation site that are necessary for initiating the transcription of RNA polymerase.

Taking Applicants' disclosure as a whole, including the above-referred-to portion, is respectfully submitted that the term "primer for introduction" sufficiently defines the metes and bounds of this aspect of the present invention such that one of ordinary skill in the art would know whether any specific primer falls within or outside the scope of the present claims. Under the present circumstances, it is respectfully submitted that the second paragraph of 35 USC 112 requires nothing more. See In re Moore, 169 USPQ 236 (CCPA 1971).

Applicants respectfully traverse the contention by the Examiner set forth in the sentence bridging pages 4 and 5 of the Office Action mailed December 29, 2005, that the description of the first base sequence "as closer to the 5' end than a third base sequence" is confusing. As indicated previously, Applicants have amended their claims to clarify what is meant by the "5' end"; and it is respectfully submitted that, particularly in view of the disclosure in Applicants' specification, and noting, e.g., Fig. 1. and the knowledge of one of ordinary skill in the art, the recitation concerning location of the first base sequence is sufficiently definite so as to satisfy the requirements of the second paragraph of 35 USC 112.

Applicants respectfully traverse contentions raised by the Examiner in the first full paragraph on page 5 of the Office Action mailed December 29, 2005, that the terms "first base sequence" and "second base sequence" are vague and indefinite. To the contrary, in view of the description of such terms in Applicants' specification, particularly as interpreted by one of ordinary skill in the art, such terms are sufficiently definite so as to satisfy the requirements of the second paragraph of 35 USC 112. Moreover, Applicants have amended claim 2 to recite that the gene to be analyzed is cDNA including the first and second base sequences introduced therein, claim 2 further defining how the sequences are introduced therein. It is respectfully submitted that this recitation, especially as presently amended, satisfies the requirements of the second paragraph of 35 USC 112.

With respect to claim 3, Applicants respectfully traverse the conclusion by the Examiner that the term "primer for introduction" is indefinite. As shown previously, in view of disclosure of such primer in the specification of the above-identified application, such term is sufficiently definite to one of ordinary skill in the art so as to satisfy the requirements of the second paragraph of 35 USC 112.

Applicants respectfully submit that all of the claims presented for consideration by the Examiner patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in the Office Action mailed December 29, 2005, that is, the teachings of the U.S. patents to Ovyn, et al, No. 6,110,681, and to Livak, et al, No. 5,538,848, United States Patent Application Publication No. US2001/0039014 to Bass, et al, and the articles by Eun, et al, "Simultaneous Quantitation of Two Orchid Viruses, by the TaqMan® Real-Time RT-PCR", in Journal of Biological Methods E7 (2000) 151-160; Leone, et al., "Molecular Beacon Probes Combined With Amplification by NASBA Enable Homogeneous,

Real-Time Detection of RNA", in Nucleic Acids Research, 1998, Vol. 26, No. 9, pages 2150-2155, and Mackay, et al., Real-Time PCR in Virology", in Nucleic Acids Research, 2002, Vol. 30, No. 6, pp. 1292-1305, under the provisions of 35 USC 103.

It is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a method for expressed gene analysis as in the present claims, having the steps of subjecting the gene to be analyzed to nucleic acid amplification using, inter alia, (a) the primer for introduction comprising a first base sequence closer to the 5' end of the primer than a third base sequence comprising a sequence specifically hybridizing to a target gene and including a second base sequence closer to the 5' end of the primer than the first base sequence, and (b) the probe comprising a base sequence identical or complementary to the first base sequence, together with steps of digesting the probe and detecting fluorescence, and wherein the gene to be analyzed is prepared by the introduction of the first base sequence and the second base sequence comprising a promoter sequence of RNA polymerase, which are nonspecific to the base sequence of the target gene, into the target gene so that the second base sequence is bound to a position closer to a 5' end of the gene to be analyzed than the first base sequence. See claim 1.

As will be shown in the following, it is respectfully submitted that none of the references disclose, or would have suggested, either alone or in combination as applied by the Examiner, a first base sequence which is nonspecific to the base sequence of the target gene or the probe as in the present claims.

In addition, it is respectfully submitted that the teachings of the references as applied by the Examiner would have neither disclosed nor would have suggested such method for expressed gene analysis as in the present claims, having features

as in claim 1 as discussed previously, and, additionally, having features as in the dependent claims, including (but not limited) wherein a gene to be analyzed is cDNA including the first and second base sequences introduced therein, as in claim 2; and/or wherein the nucleic acid amplification is conducted by steps as in claims 3 and 4; and/or wherein the nucleic acid amplification is conducted at a substantially single temperature (see claim 5), in particular where such single temperature is between 37°C and 55°C (see claim 6); and/or wherein the RNA polymerase and the second base sequence are as set forth in claim 7; and/or wherein 2 or more target genes are simultaneously detected in a single reaction vessel using at least two types of probes (see claim 8), in particular wherein such at least two types of probes have substantially the same melting temperature (see claim 9); and/or wherein the probe is a DNA/RNA hybrid strand (see claim 14).

By use of the primer for introduction as in the present claims, which includes the first, second and third base sequences relatively located to the 5' end of the primer, with the first base sequence and the second base sequence being nonspecific to the base sequence of the target gene, together with the probe comprising a base sequence identical or complementary to the first base sequence, a universal probe for expressed gene analysis which does not have to be designed for each use in accordance with the base sequence of the target gene is achieved. The probe according to the present invention can amplify and detect any type of target genes under substantially the same conditions, and analysis thereof can be simply conducted. Note, for example, the second paragraph on page 6 of Applicants' specification; see also the paragraph bridging pages 28 and 29 thereof.

Ovyn, et al. discloses oligonucleotides that can be used as primers to amplify a region of the 16S rRNA of *Mycoplasma pneumoniae*. Note column 3, lines 39-45

of this patent. Note especially column 7, lines 5-28, of this patent, describing a method for the detection of the specified microorganism. Note also column 3, lines 39-46; column 5, lines 46-67; and column 6, lines 12-16 and 43-61.

It is respectfully submitted that Ovyn, et al. would have neither taught nor would have suggested the presently claimed method, including, inter alia, a first base sequence which is nonspecific to the base sequence of the target gene.

The Examiner contends that Ovyn, et al. teaches nucleic acid amplification using a primer for introduction comprising first and second base sequences corresponding to those in the present claims. However, it is respectfully submitted that the upstream and downstream primers in Ovyn, et al. only comprise, respectively, a sequence substantially complementary to the target sequence and a sequence substantially homologous to the target sequence. It is respectfully submitted that this patent would have neither taught nor would have suggested, inter alia, a first base sequence as in the present claims.

The additional contention by the Examiner on page 6 of the Office Action mailed December 29, 2005, that Ovyn, et al. teaches a probe including a base sequence identical or complementary to the first base sequence and labeled at one end with a fluorophore, is respectfully traversed. It is respectfully submitted that the probe described in Ovyn, et al. does not include "a base sequence identical or complementary to the first base sequence". It is respectfully submitted that Ovyn, et al. would have neither taught nor would have suggested such probe including such base sequence identical or complementary to the first base sequence, as in the present claims.

It is respectfully submitted that the teachings of the secondary references as applied by the Examiner would not have rectified the deficiencies of Ovyn, et al.,

such that the presently claimed invention as a whole would have been obvious to one or ordinary skill in the art.

Livak, et al. discloses methods of monitoring the process of nucleic acid amplification reactions, especially polymerase chain reactions. Note, in general, column 3, lines 29-47, for the broadest description of this method. See also column 3, lines 48-55.

Eun, et al. discloses simultaneous quantitation of two orchid viruses carried out using the TaqMan® real-time RT-PCR. As for the primer design for the method disclosed in Eun, et al., note Table 1 and the description in Item 2.2 on page 153 of this article.

Even assuming, arguendo, that the teachings of Livak, et al. and of Eun, et al. were properly combinable with the teachings of Ovyn, et al., such combined teachings would have neither disclosed nor would have suggested the presently claimed subject matter, including, inter alia, the base sequences, including in particular wherein the first and second base sequences are nonspecific to the base sequence of the target gene, and/or the probe including a base sequence identical or complementary to the first base sequence, and advantages achieved thereby; and/or other features of the present invention as discussed in the foregoing, and advantages thereof.

It is respectfully submitted that the teachings of the references as applied by the Examiner in Items 5 and 6 on pages 10-14 of the Office Action mailed December 29, 2005, would have neither taught nor would have suggested the presently claimed subject matter, including features thereof as discussed previously.

The article by Leone, et al. in Nucleic Acids Research (hereinafter "Leone") discloses employment of molecular beacon probes in a NASBA amplicon detection system to generate a specific fluorescent signal concomitantly with amplification. This article describes the coupling of RNA amplification by NASBA with amplicon detection by molecular beacons technology to produce a homogenous RNA assay, called AmpliDet RNA. Note the first full paragraph in the left-hand column on page 2151 of this article. See also the discussions under the headings "Selection of amplification primers and probe", "Synthesis of the molecular beacons", "NASBA" and "Post-NASBA analysis", on page 2151 of this article.

It is respectfully submitted that Leone would have neither taught nor would have suggested the presently claimed subject matter, including, inter alia, the first base sequence and probe as in the present claims and discussed previously.

The contention by the Examiner on page 10 of the Office Action mailed December 29, 2005, that Leone teaches a primer for introduction including a first base sequence closer to the 5' end than a third base sequence comprising a sequence specifically hybridizing to a target gene and comprising a second base sequence closer to the 5' end than the first base sequence, is noted. However, it is respectfully submitted that Leone only describes secondary structure models of NASBA amplicons produced by a specified primer set, with each amplicon also containing at its 5' end the transcription initiation sequence from specified primers for the T7 RNA polymerase. It is respectfully submitted that Leone does not describe a primer comprising "a first base sequence" which is nonspecific to the base sequence of the target gene. Thus, it is respectfully submitted that Leone would have neither taught nor would have suggested the primer for introduction as in the present invention, which includes the first base sequence.

On page 11 of the Office Action mailed December 29, 2005, the Examiner contends that Leone discloses a probe including a base sequence identical or complementary to the first base sequence and labeled at one end with a fluorophore. However, it is respectfully submitted that the probe in Leone does not include a base sequence identical or complementary to the first base sequence, and would have neither taught nor would have suggested a probe comprising such base sequence identical or complementary to the first base sequence, as in the present claims.

Reference by the Examiner to the article by Leone, et al., in the Journal of Virological Methods, in the sentence bridging pages 10 and 11 of the Office Action mailed December 29, 2005, is noted. It is emphasized that the Examiner has not set forth this article in the formal statement of the rejection, and has not satisfied requirements of 35 USC 103 (including showing motivation) in connection with this article. If the Examiner intends to maintain reliance on this article, it must be set forth in the formal statement of the rejection and analyzed under requirements of 35 USC 103. See In re Hoch, 166 USPQ 406, 407 n.3 (CCPA 1970).

While it is respectfully submitted that Applicants need not presently address contentions made by the Examiner with respect to the article by Leone, et al. in the Journal of Virological Methods, the following is noted. Thus, in this article, there is only a description that the sense primers were entirely target specific, whereas the antisense primers consisted of a 3' terminal, target specific sequence and a 5' terminal T7 promoter sequence. See page 21, Section 2.2. It is respectfully submitted that this article does not describe, nor would have suggested, either alone or in combination with the teachings of the other applied references, a primer including a first base sequence which is nonspecific to the base sequence of the target gene. Thus, it is respectfully submitted that the primer described in this article

is entirely different from the primer for introduction of the present invention, which includes the specified first base sequence.

It is respectfully submitted that the secondary references applied by the Examiner in Item 5 on page 10 of the Office Action mailed December 29, 2005, would not have rectified the deficiencies of Leone, such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Bass, et al. discloses automated devices and systems for performing nucleic acid recombination, mutation, shuffling and other diversity generating reactions in vitro. As applied by the Examiner, this publication discloses that as an alternative to TaqMan® is the use of molecular beacons to assess library quality. Note paragraph [0329] on page 36.

Mackay reports on detection of polymerase chain reaction products during real-time. As applied by the Examiner, note, for example, page 1297, right-hand column, of this article.

Even assuming, arguendo, that the teachings of Leone, Bass, et al. and Mackay, et al. were properly combinable, it is respectfully submitted that such combined teachings would have neither disclosed nor would have suggested the presently claimed subject matter, including the first base sequence, nonspecific to the base sequence of the target gene, and other features of the present invention as discussed previously, including the probe with a base sequence identical or complementary to the first base sequence, and advantages thereof.

In view of the foregoing comments and amendments, reconsideration and allowance of all claims presently in the application are respectfully requested.

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Respectfully submitted,

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